UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/350,899	07/12/1999	KOUICHI TSUJI	029650-080	8923

21839 7590 07/02/2002

BURNS DOANE SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	13

DATE MAILED: 07/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/350,899	Tsuji et al
Examiner	**Art Unit**
Karen Canella	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is FINAL. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-12 and 15* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-12 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some* c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Arguments

1. The finality of the Office action of Paper No. 13 is withdrawn

2. Claims 10-12 and 15 are under consideration

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections Maintained

4. The rejection of claims 10 and 11 under 35 U.S.C. 102(b) as being anticipated by Stein et al (Hybridoma, 1988, Vol. 7, pp. 555-567) is maintained for reasons of record. Applicant argues that the antigen disclosed by Stein et al cannot be the antigen of the instant invention as Stein et al used a membrane preparation of the Calu3 cell line to raise antibodies to said antigen in contrast to the instant invention which used secreted antigen from the Calu3 cell line. This has been considered but not found persuasive. The antibodies generated in the instant application, although raised from cell culture medium comprising a secreted or shed glycoprotein, are able to bind antigen on the surface of human lung adenocarcinoma teaching against the notion that the disclosed antigens are only present in the extracellular milieu and not present on the cell membrane. Further, use of a membrane preparation does not exclude the presence of secreted antigens as said antigens must pass through the cellular membrane during the process of secretion, and are therefore at some point part contained within the membrane. See De Robertis, (cited in a previous Office action) page 237, the legend for Figure 11-7 which states "The glycoproteins are transported from the Golgi by carrier vesicles and released by exocytosis *at the plasma membrane*". A cell which is actively secreting a glycoprotein will have said glycoprotein passing through the plasma membrane. It is reasonable to conclude that the membrane preparation of Stein et al contained said antigen. In addition, the antigen disclosed by Stein et al is present in lung adenocarcinoma tumor tissue (Table 1) at high levels, which is characteristic of instant antigen as disclosed by the specification. Applicant argues that the antibody of Stein et al is of the IgG isotype and the instant antibodies are of the IgM isotype and therefore do not define the same claimed antigen. However the isotype of the antibodies which bind to the

claimed antigen is not a property of the claimed antigen as isotypes define the non-antigen binding effector region of an antibody, and do not contribute to binding an antigenic determinant. Roitt et al teach that antibodies can vary in idiotype, and isotype (page 4.7, second column and legend for figure 4.16) and that the specific idiotope determines the specificity of antigen binding (page 4.8, second column, lines 1-4). Roitt et al further teach that the isotype of an antibody determines the class and subclass of said antibody (legend for figure 4.16) and that the class and subclass of an antibody influences complement fixation (legend for figure 4.17), and the ability to bind to receptors on mononuclear cells, neutrophils and mast cells (legend for figure 4.18). Thus, the IgG antibody disclosed by Stein et al does not teach away from the instant antigen bound by an IgM antibody as the art teaches that the class of an antibody does not influence the antigen binding site of said antibody.

New Grounds of Rejection

5. Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stein et al (Hybridoma, 1988, Vol. 7, pp. 555-567) in view of Wands et al (US 5,422,239).

Stein et al teaches the invention of claims 10 and 11 for the reasons set forth above.

Claim 12 is drawn in part to a method for the diagnosis of human lung adenocarcinoma which comprises contacting a sample suspected of containing human lung adenocarcinoma cells with a diagnostically effective amount of monoclonal antibody produced by the hybridomas of FERM BP-5383, FERM P-14879, FERM P-14880, said antibody being of the IgM class and determining whether said sample contains human adenocarcinoma cells based on the binding of the glycoprotein antigen in said sample to said monoclonal antibody. Stein et al disclose a method of diagnosing human lung adenocarcinoma comprising contacting the RS5-46 antibody which binds to the disclosed antigen from Calu3 cells, to tumor tissue sections (pages 560-561 under the heading, "Immunoperoxidase Staining of Frozen tissue Sections" and figure 1, page 562). Stein et al do not teach an antibody which binds to the disclosed antigen from Calu3 cells which is of the IgM class as the RS5-46 antibody is of the IgG class.

Wands et al teach the use of monoclonal antibodies of the IgM class having high affinity

for antigen in an immunoassay. Wands et al teach (column 4, lines 62-66) that IgM antibodies obtained through hybridoma technology, can detect less antigen than IgM antibodies obtained from endogenous sources. In the table of column 9, Wands et al compares the binding of an IgG anti-hepatitis B antibody with a IgM anti-hepatitis-B antibody with respect to the total binding and the signal to noise ratio and concludes that an improvement was effected by substitution of the IgM antibody for the IgG antibody (legend heading table). Wands et al also teach that IgM class antibodies can bind antigen at a faster rate than IgG antibodies (column 8, lines 60-62).

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to make an IgM antibody which binds to the Calu3 antigen taught by Stein et al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Wands et al on the greater sensitivity, greater signal to noise ratio and faster binding of antigen effected by substitution of hybridoma-produced IgM antibodies for monoclonal IgG antibodies in an immunoassay.

6. Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taniguchi et al (EP 232,871, 1987) in view of Stein et al.

The embodiment of claims 10-12 are set forth above.

Taniguchi et al teach a method of for the diagnosis of human lung adenocarcinoma which comprises contacting a sample suspected of containing human lung adenocarcinoma cells with a diagnostically effective amount of monoclonal antibody 4G12, said antibody being of the IgM class, and determining whether said sample contains human adenocarcinoma cells based on the binding of the glycoprotein antigen in said sample to said monoclonal antibody (page 6, lines 16-45). Taniguchi et al do not teach the antigen of claims 10 and 11 as the antigen of Taniguchi et al appears to have a molecular weight of 65 kDa on reducing SDS gel electrophoresis.

Stein et al teach the antigen of claims 10 and 11 for the reasons set forth in the Office action of Paper No. 8, and the reasons set forth in section X, above.

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute the antigen of Stein et al for the antigen of Taniguchi et

al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Stein et al on the presence of the Calu3 antigen in human adenocarcinoma tumors.

7. Claims 12 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jost et al (5,888,773) in view of Stein et al. Claim 12 is drawn in part to a method for the diagnosis of human lung adenocarcinoma which comprises contacting a sample suspected of containing human lung adenocarcinoma cells with a diagnostically effective amount of a fragment of a monoclonal antibody produced by the hybridomas of FERM BP-5383, FERM P-14879, FERM P-14880, and determining whether said sample contains human adenocarcinoma cells based on the binding of the glycoprotein antigen in said sample to said monoclonal antibody. Claim 15 specifies that the fragment is a Fab, F(ab)2 or Fv fragment. Jost et al teach an immunoassay for a tumor marker using an Fv antibody fragment (column 13, lines 9-11). Joste et al further teach that said Fv fragments retain the antigen binding function of the parental antibody (column 1, lines 10-15). Jost et al do not teach Fc fragments that bind to the instant antigen.

Stein et al teach the instant antigen, the IgG antibody which binds thereto and an immunoassay for the detection of lung adenocarcinoma comprising the use of the RS-46 IgG antibody..

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute the Fv fragment of the RS5-46 antibody for the general Fv fragment as taught by Jost et al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Stein et al on the binding of the RS-46 antibody to lung adenocarcinoma tissues and the lack of binding of said antibody to normal fibroblasts.

8. Claims 10-12 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jost et al (5,888,773) and Stein et al as applied to claims 10-12 and 15 above, and further in view of Holtlund et al (US 5,650,333). The embodiments of the claims have been set forth above. Claim

15 additionally embodies Fab and F(ab)2 fragments of the antibodies of claim 12. Neither Jost et al nor Stein et l teach Fab and F(ab)2 fragments.

Holtlund et al teach the use of Fab and F(ab)2 fragments in immunoassays.

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute a Fab or F(ab)2 fragment for the Fv fragment as taught by the combination of Jost et al and Stein et al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Holtlund et al on the equivalence of Fab and F(ab)2 fragments with whole immunoglobulins such as IgG or IgM in the immunoassay taught (column 5, line 60 to column 6, line 4).

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
June 18, 2002